REMARKS

This Amendment is being presented in connection with the filing of the above-identified application which is a national phase application of the above-identified international (PCT) application. A substitute specification is being submitted concurrently with this Amendment and the above-identified application. This substitute specification is in accordance with the translation of the originally filed international application including the specification and claims; and an Abstract of the Disclosure (added as page 48 based on the abstract that was included in the published International Application (Publication No. WO 01/18198 A1)). In addition, seven (7) drawing sheets are being submitted concurrently with this Amendment and the above-identified application for use in connection with the above-identified application. These sheets are in accordance with the drawings appearing in International Publication No. WO 01/18198 A1.

With respect to the above amendments to the specification, subtitles have been added in order to conform the application to the requirements for applications of the United States Patent and Trademark Office. With respect to the above amendments to the claims, the claims have been amended principally so that each of the claims is dependent on a single claim rather than on multiple claims.

In accordance with 37 C.F.R. §§1.821-1.825, a sequence listing of 98 pages is being currently submitted herewith. This sequence listing is the listing submitted with the above-identified international application, but does incorporate the above amendments to line <110> (where the inventors were substituted for the assignee) and line <130> (where the attorney docket number for the above-identified national phase application was substituted for the attorney docket number of the international application). In further conformity with 37 C.F.R. §1.824, the sequence listing, as amended above, is being provided in computer readable form an a diskette in conformity with 37 C.F.R. §1.824(c)(1).

Respectfully submitted,
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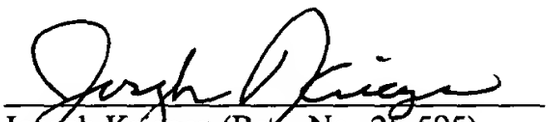
By 

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Version of Amended Claim with Markings to Show Changes Made

The following is a marked up version of claims showing the amendments made to that claim (the changes are shown by underlining added matter and striking through deleted matter):

IN THE CLAIMS

Rewrite claims 3-5, 8-10, 12-19, 21, 23-26, and 29-36 as follows:

3. (amended) Purified or isolated nucleic acid according to claim 1~~ or 2~~, characterized in that it comprises at least one sequence of at least 15 consecutive nucleotides of the nt 714-809, ends inclusive, fragment of the sequence SEQ ID No. 2, of the sequence complementary thereto or of the sequence of the corresponding RNA thereof.

4. (amended) Purified or isolated nucleic acid according to ~~one of claims 1 to 3~~claim 1, characterized in that it comprises a mutation corresponding to a natural polymorphism in humans.

5. (amended) Probe or primer, characterized in that it comprises a sequence of a nucleic acid according to ~~one of claims~~claim 1~~ to 4~~.

8. (amended) Method for screening cDNA or genomic DNA libraries, or for cloning isolated genomic or cDNA encoding spastin, characterized in that it uses a nucleic acid sequence according to ~~one of claims~~claim 1 ~~to 7~~.

9. (amended) Method according to claim 8, for identifying the genomic or cDNA sequence of the SPG4 gene of mammals~~, in particular of mice~~.

10. (amended) Method for identifying a mutation carried by the human SPG4 gene, characterized in that it uses a nucleic acid sequence according to ~~one of claims~~claim 1 ~~to 7~~.

12. (amended) Method for identifying the nucleic acid sequences which promote and/or regulate the expression of the SPG4 gene, characterized in that it uses a nucleic acid sequence according to ~~one of claims~~claim 1 ~~to 7~~.

13. (amended) Nucleic acid identified using a method according to ~~one of claims~~claim 9 ~~to 12~~.

14. (amended) Polypeptide encoded by a nucleic acid according to ~~one of claims~~claim 1 ~~to 4 and 13~~.

15. (amended) Polypeptide according to claim 14, ~~preferably~~ with the exception of the 584 amino acid peptide, the sequence of which is identified in the GenBank databank under the accession number AB029006.

16. (amended) Polypeptide according to claim 14 ~~or 15~~, characterized in that it comprises an amino acid sequence chosen from the group comprising:

a) the sequence SEQ ID No. 3, the sequence SEQ ID No. 73, the sequence SEQ ID No. 107 or the sequence of at least 10 consecutive amino acids of one of these sequences; and

b) the sequences which are homologs or variants of the sequences SEQ ID No. 3, SEQ ID No. 73 or SEQ ID No. 107.

17. (amended) Polypeptide according to claim 14 ~~or 15~~, characterized in that it comprises the sequence of at least 8 consecutive amino acids of the sequence of the aa 197-228, ends inclusive, fragment of the sequence SEQ ID No. 3.

18. (amended) Polypeptide according to claim 14 ~~or 15~~, characterized in that it comprises an amino acid sequence chosen from the group comprising the sequence SEQ ID No. 3, the sequence SEQ ID No. 73, the sequence SEQ ID No. 107, which sequences carrying at least one of the mutations corresponding to a natural

polymorphism in humans, and the sequences of the fragments thereof of at least 10 consecutive amino acids.

19. (amended) Cloning and/or expression vector containing a nucleic acid sequence according to ~~one of claims~~claim 1 ~~to 4, and 13~~.

21. (amended) Host cell transformed with a vector according to claim 19 ~~or 20~~.

23. (amended) Mammal, except a human, according to claim 22, comprising a transformed cell, characterized in that the sequence of at least one of the two alleles of the SPG4 gene contains at least one of the mutations corresponding to a natural polymorphism in humans ~~or identified using a method according to claim 10 or 11~~.

24. (amended) Use of a nucleic acid sequence according to ~~one of claims~~claim 5, ~~6 and 13,~~ as a probe or primer, for detecting and/or amplifying nucleic acid sequences.

25. (amended) Use of a nucleic acid sequence according to ~~one of claims~~claim 1 ~~to 7, and 13~~, for screening a genomic or cDNA library.

26. (amended) Use of a nucleic acid sequence according to ~~one of claims~~claim 1 ~~to 4 and 13~~, for producing a recombinant or synthetic polypeptide.

29. (amended) ~~Mono-~~Monoclonal or polyclonal antibodies or their fragments, chimeric antibodies or immunoconjugates, characterized in that they are capable of specifically recognizing a polypeptide according to ~~one of claims~~claim 14 ~~to 18, and 28~~.

30. (amended) Method for detecting and/or purifying a polypeptide ~~according to one of claims 14 to 18, and 28~~, characterized in that it uses an antibody according to claim 29.

31. (amended) Method for genotypic diagnosis of AD-HSP associated with the SPG4 gene, characterized in that a nucleic acid sequence according to ~~one of claims~~claim 1 ~~to 7 and 13~~ is used.

32. (amended) Method for genotypic diagnosis of AD-HSP associated with the presence of at least one mutation on a sequence of the SPG4 gene, using a biological sample from a patient, characterized in that it includes the following steps:

a) where appropriate, isolation of the genomic DNA from the biological sample to be analyzed, or production of cDNA from the RNA of the

biological sample;

b) specific amplification of said DNA sequence of the SPG4 gene likely to contain a mutation, using primers according to ~~either of claims~~claim 5 ~~and 6 or a nucleic acid according to claim 13~~;

c) analysis of the amplification products obtained and comparison of their sequence with the corresponding normal sequence of the SPG4 gene.

33. (amended) Method for diagnosing AD-HSP associated with abnormal expression of a polypeptide encoded by the SPG4 gene, characterized in that one or more antibodies according to claim 29 is ~~(are)~~ brought into contact with the biological material to be tested, under conditions which allow the possible formation of specific immunological complexes between said polypeptide and said antibody ~~or antibodies~~, and in that the immunological complexes possibly formed are detected and/or quantified.

34. (amended) Method for selecting a chemical or biochemical compound which is capable of ~~interacting directly or indirectly with a polypeptide according to one of claims 14 to 18, and 28, or with a nucleic acid according to one of claims 1 to 7, and 13, and/or which makes it possible to modulate~~modulating the

expression or the activity of ~~these~~ a ~~polypeptides~~polypeptide encoded by the 5PG4 gene, characterized in that it comprises bringing a nucleic acid sequence according to ~~one of claims~~claim 1 ~~to 7, and 13, a polypeptide according to one of claims 14 to 18, and 28, a vector according to either of claims 19 and 20, a cell according to claim 21, a mammal according to either of claims 22 and 23 or an antibody according to claim 29~~ into contact with a candidate compound, and detecting a modification of the activity of said polypeptide.

35. (amended) Use of a nucleic acid sequence according to ~~one of claims~~claim 1 ~~to 7, and 13, of a polypeptide according to one of claims 14 to 18, and 28, of a vector according to either of claims 19 and 20, of a cell according to claim 21, of a mammal according to either of claims 22 and 23 or of an antibody according to claim 29~~, for studying the expression or the activity of the SPG4 gene.

36. (amended) Kit ~~or pack~~ for diagnosis, characterized in that it comprises at least ~~one compound chosen from the following group of compounds:~~

~~a) a nucleic acid according to either of claims~~claim 5 ~~and 6;~~

~~and~~

~~b) an antibody according to claim 29~~.